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Supplemental Material

Evaluating the Effect of Gestational Exposure to Perfluorohexane Sulfonate on Placental Development in Mice Combining Alternative Splicing and Gene Expression Analyses

Yihao Zhang, Jia Lv, Yi-Jun Fan, Lin Tao, Jingjing Xu, Weitian Tang, Nan Sun, Ling-Li Zhao, De-Xiang Xu, and Yichao Huang

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Figure S1. Experimental animal phenotype. PFHxS exposure from GD7 to GD17 for pregnant mice (mean ± SEM). The exposure dose were 0.3 (High) and 0.03 (Low) μg/kg/day, which were administered in corn oil with 0.1% DMSO; and the Control was corn oil with 0.1% DMSO. (A) Maternal weight; (B) Food consumption; (C) Liver/Body weight ratio; (D) Brain/Body weight ratio; (E) Liver births per litter. $N = 6$ in each group, P values were determined by One-way Analysis of Variance, all $P > 0.05$. Data in (A-E) are also presented in Excel Table S18. Notes: DMSO, dimethyl sulfoxide; GD, gestational day; PFHxS, perfluorohexane sulfonate; SEM, Standard Error of Mean.

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Figure S3. Signal pathways in multiple biological processes of placental development in response to PFHxS exposure. (A) Heatmap showing the DEGs profile of development gene set between high-dose group and control. (B) Heatmap showing the DEGs profile of metabolic process gene set between high-dose group and control. (C) Heatmap showing the DEGs profile of proliferation gene set between high-dose group and control. (D) Heatmap showing the DEGs profile of transport gene set between high-dose group and control. (E) GSEA showing the positive enrichment of TGF β signaling pathway in high-dose group compare to control. (F) GSEA showing the positive enrichment of p53 signaling pathway in high-dose group compare to control. (G) GSEA showing the positive enrichment of Wnt signaling pathway in high-dose group compare to control. (H) UpSetR plot showing the number of unique and shared DEGs between development, proliferation, metabolic process and transport gene sets. (I) Circos plot showing GO analysis of shared DEGs for 4 gene sets. $N = 6$ in each group, including 3 males and 3 females. *P* and FDR values were determined by permutation test and Benjamini-Hochberg method (E, F and G), respectively. Data in (A-I) are also presented in Excel Table S20. Notes: DEGs, differentially expressed genes; FDR, false discovery rate; GSEA, gene set enrichment analysis; PFHxS, perfluorohexane sulfonate.

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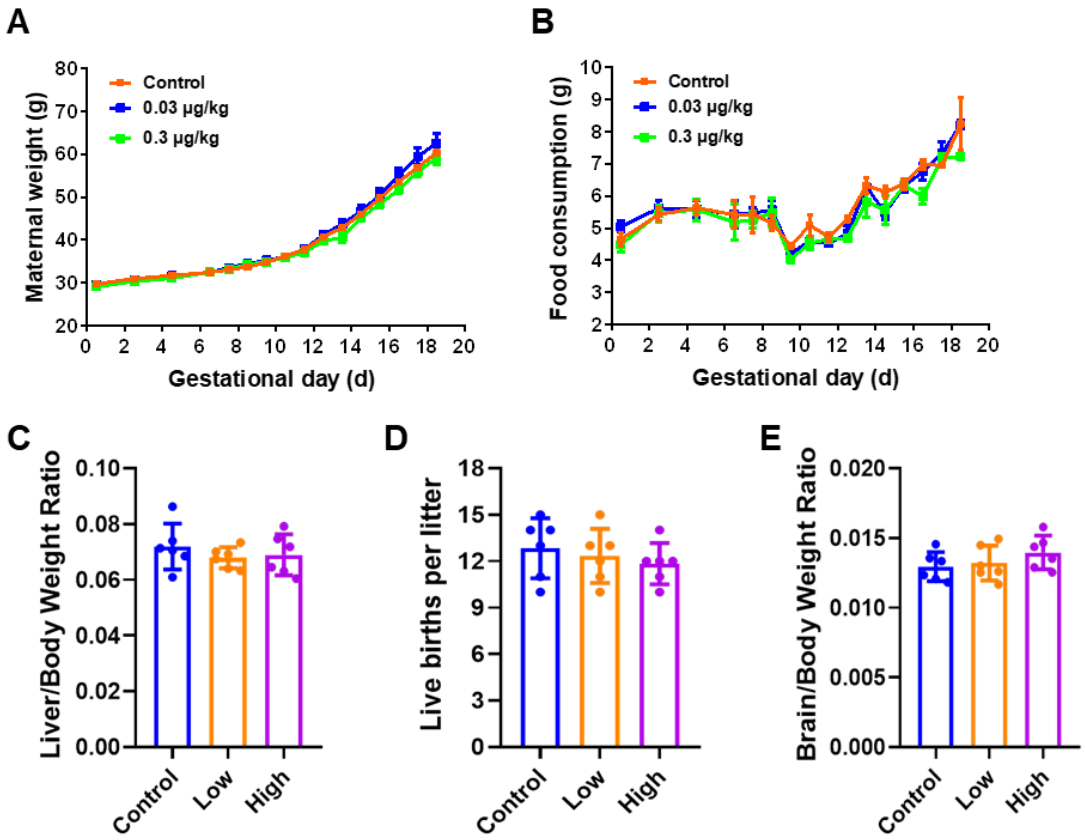
Additional File- Excel Document



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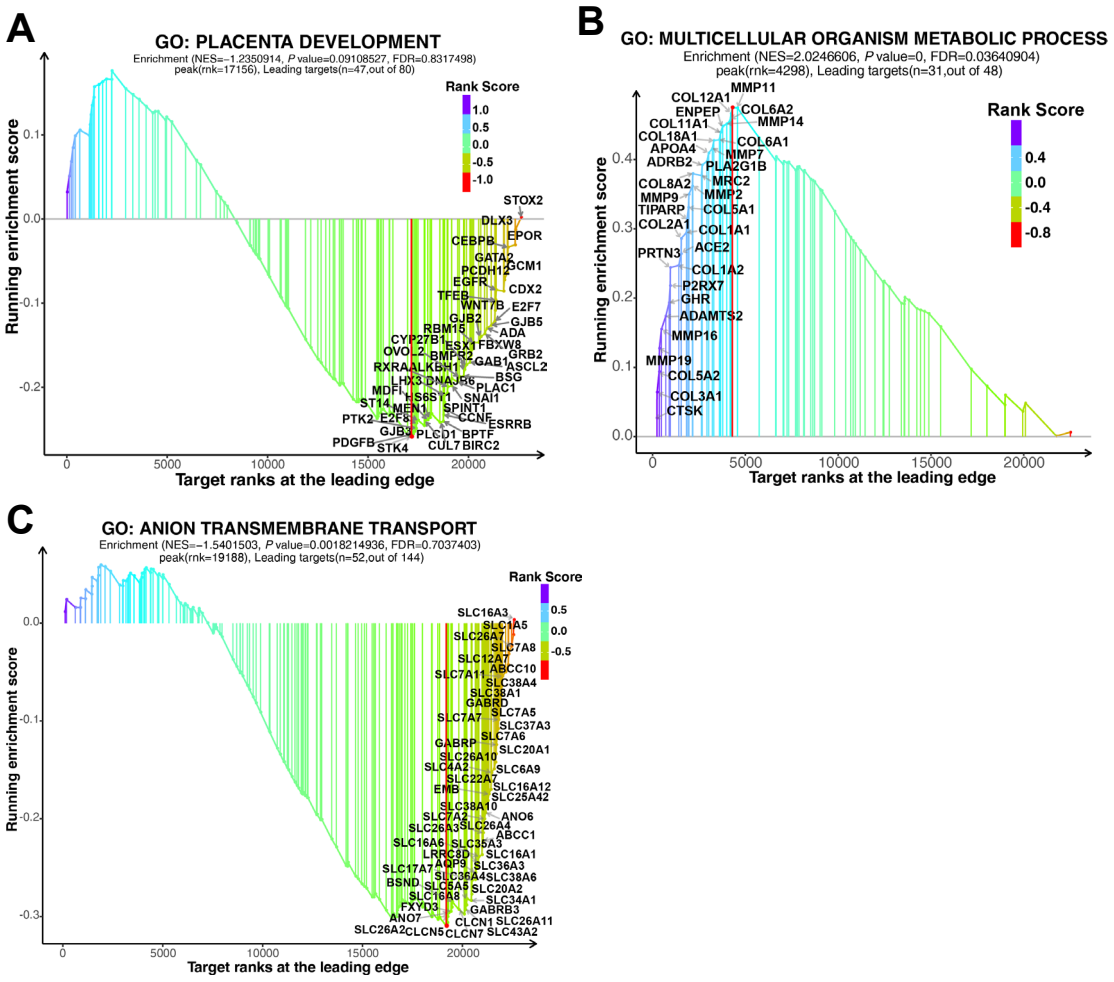

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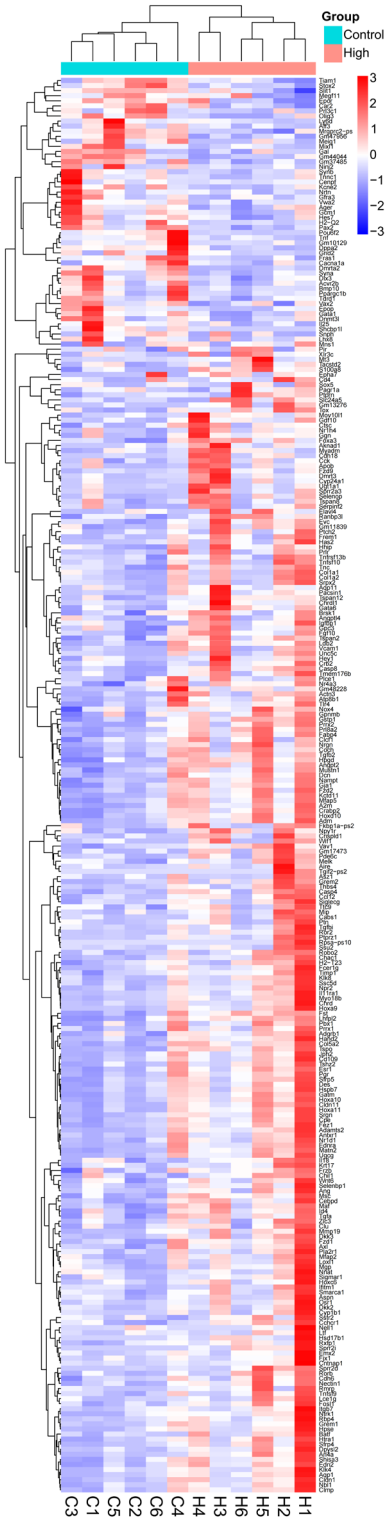
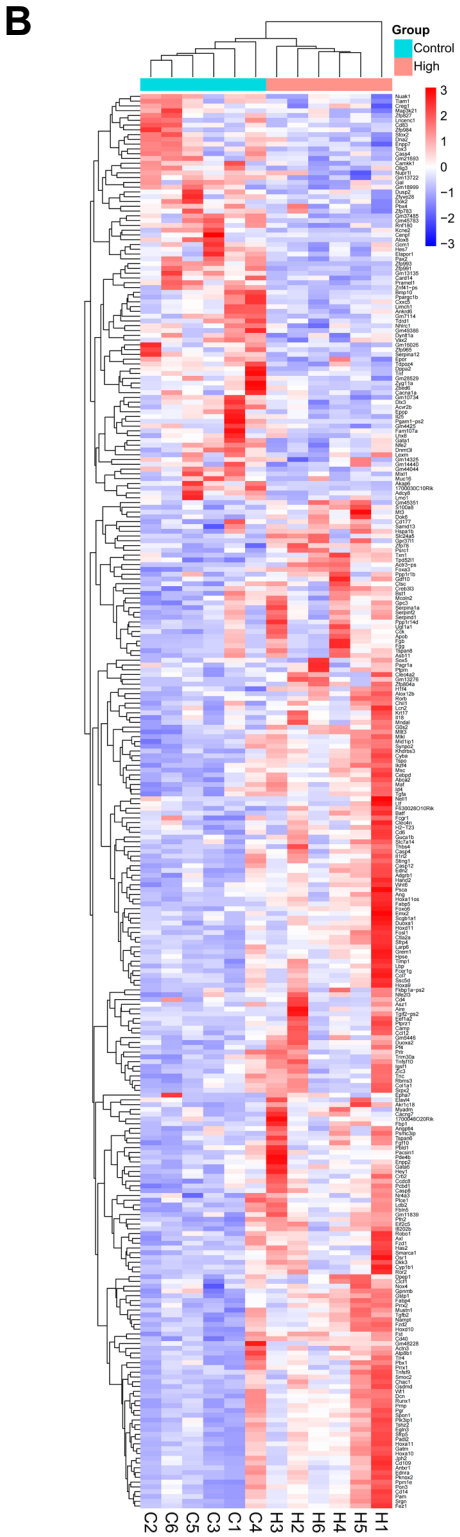
A

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2
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C5
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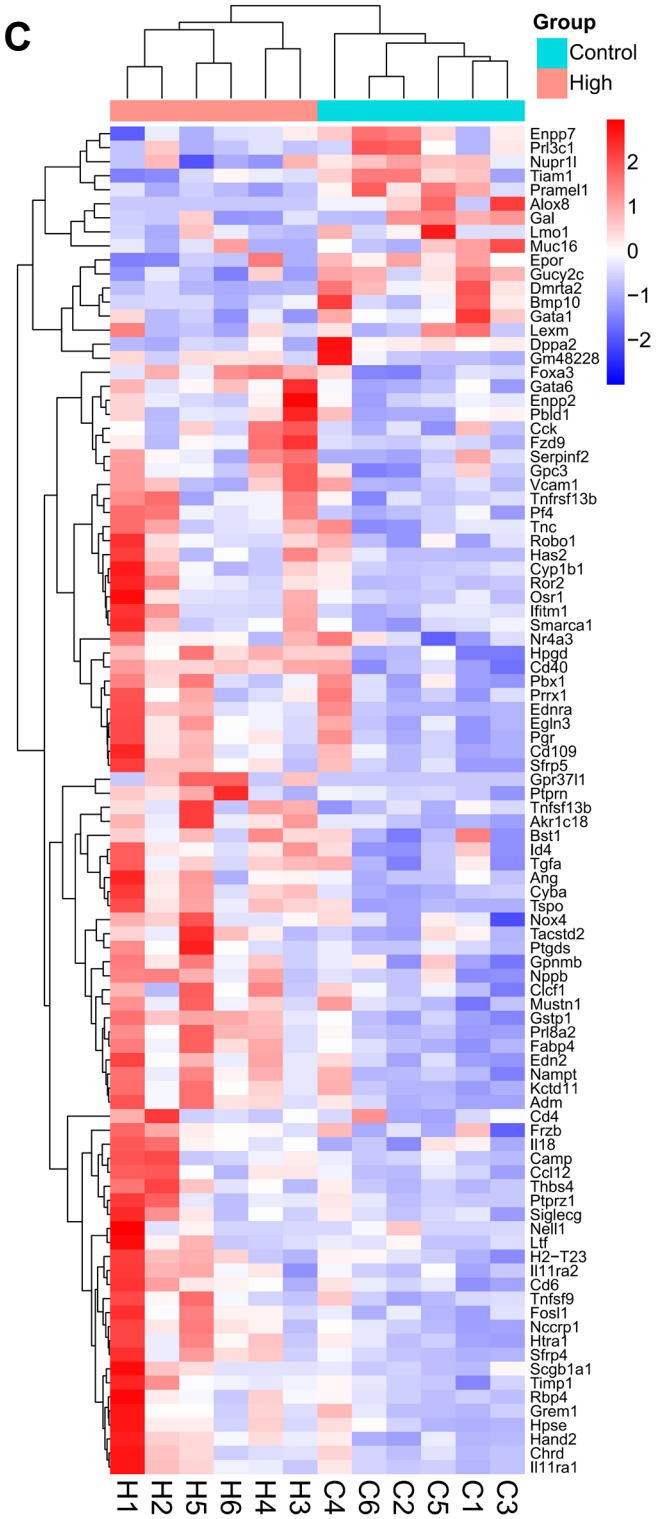
C1
C4
H3
H2
H6
H4
H5
H1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Gal
Lmo1
Muc16
Epor
Gucy2c
Dmrta2
Bmp10
Gata1
Lexm
Dppa2
Gm48228
Foxa3
Gata6
Enpp2
Pbld1
Cck
Fzd9
Serpinf2
Gpc3
Vcam1
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Pf4
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Robo1
Has2
Cyp1b1
Ror2
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Ifitm1
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Nampt
Kctd11
Adm
Cd4
Frzb
Il18
Camp
Ccl12
Thbs4
Ptprz1
Siglecg
Nell1
Ltf
H2−T23
Il11ra2
Cd6
Tnfsf9
Fosl1
Nccrp1
Htra1
Sfrp4
Scgb1a1
Timp1
Rbp4
Grem1
Hpse
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H4
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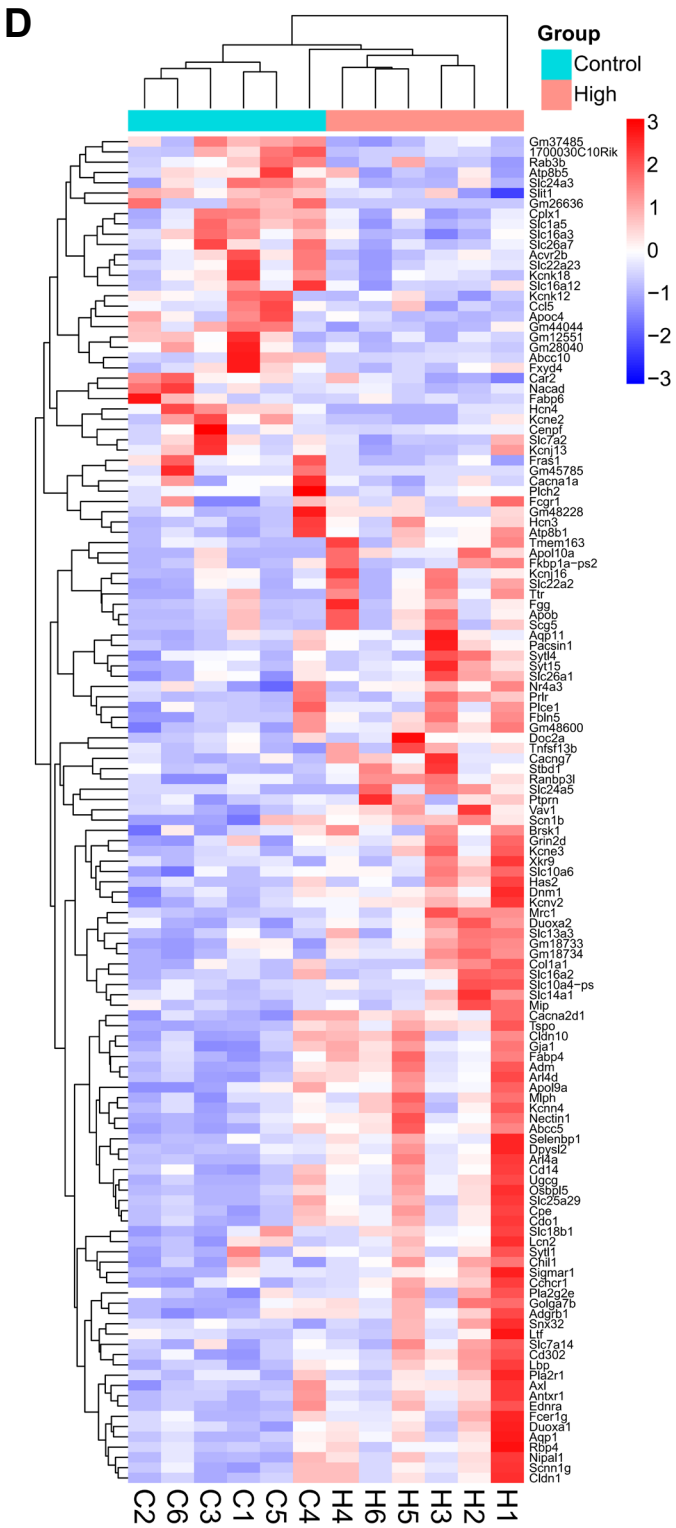
C6
C2
C5
C1
C3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Acvr2b
Slc22a23
Kcnk18
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Cenpf
Slc7a2
Kcnj13
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Gm48228
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Ttr
Fgg
Ab0b
Scg5
Aqp11
Pacsin1
Sytl4
Syt15
Slc26a1
Nr4a3
Prlr
Plce1
Fbln5
Gm48600
Doc2a
Tnfsf13b
Cacng7
Stbd1
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Kcnv2
Mrc1
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Cacna2d1
Tspo
Cldn10
Gja1
Fabp4
Adm
Ar4d
Apol9a
Mlph
Kcnn4
Nectin1
Abcc5
Selenbp1
Dpysl2
Ar4a
Cd14
Ugcg
Obbpl5
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Cd302
Lbp
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Axl
Antxr1
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Nipal1
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C1
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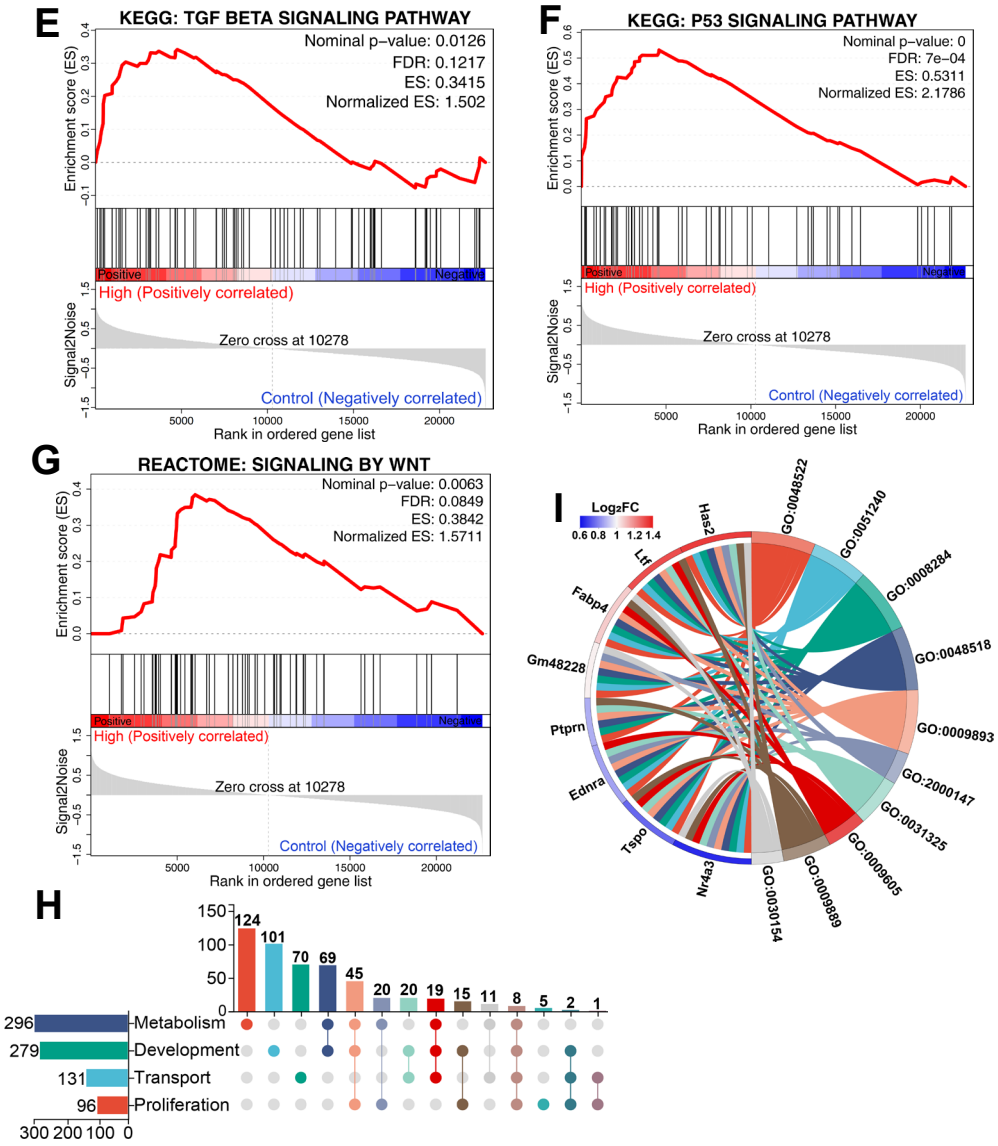

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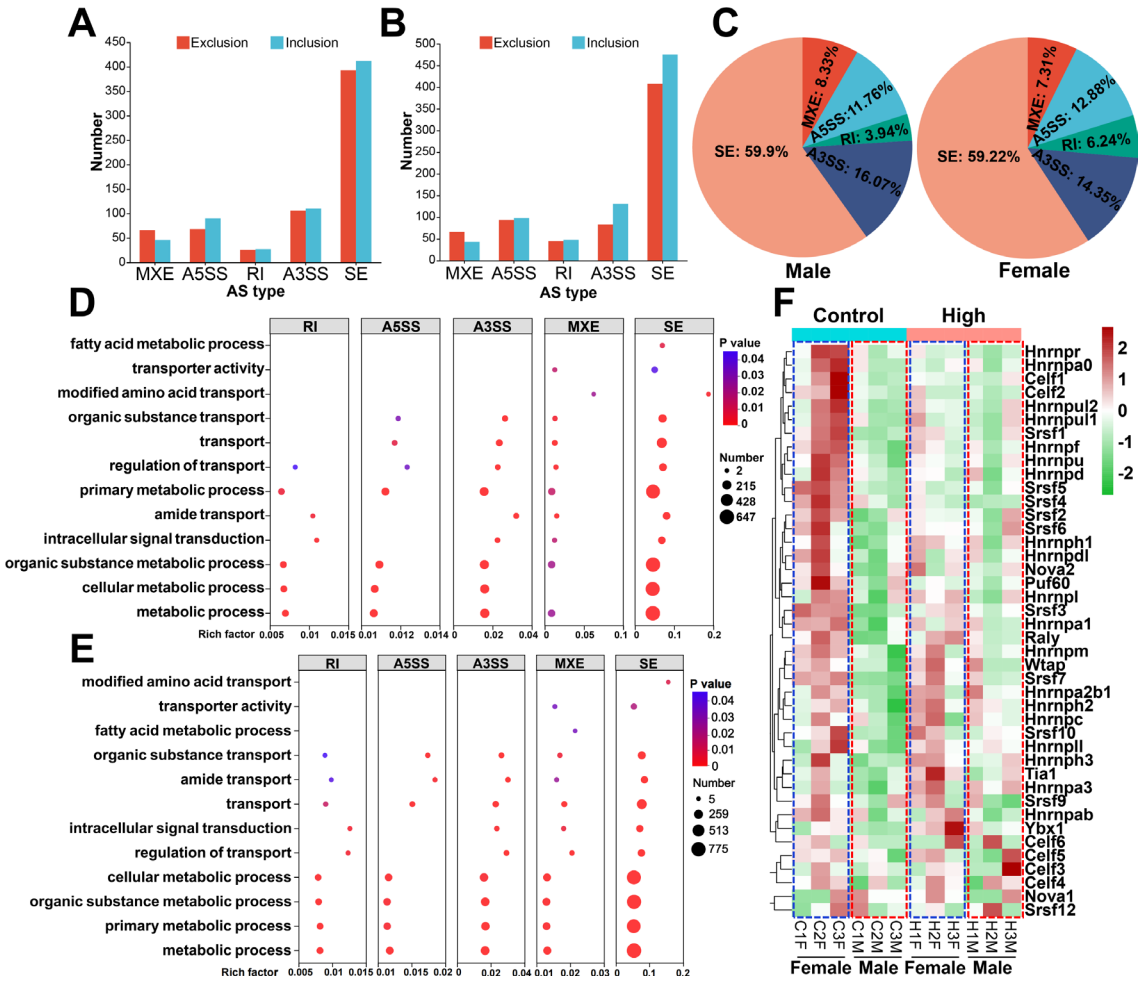

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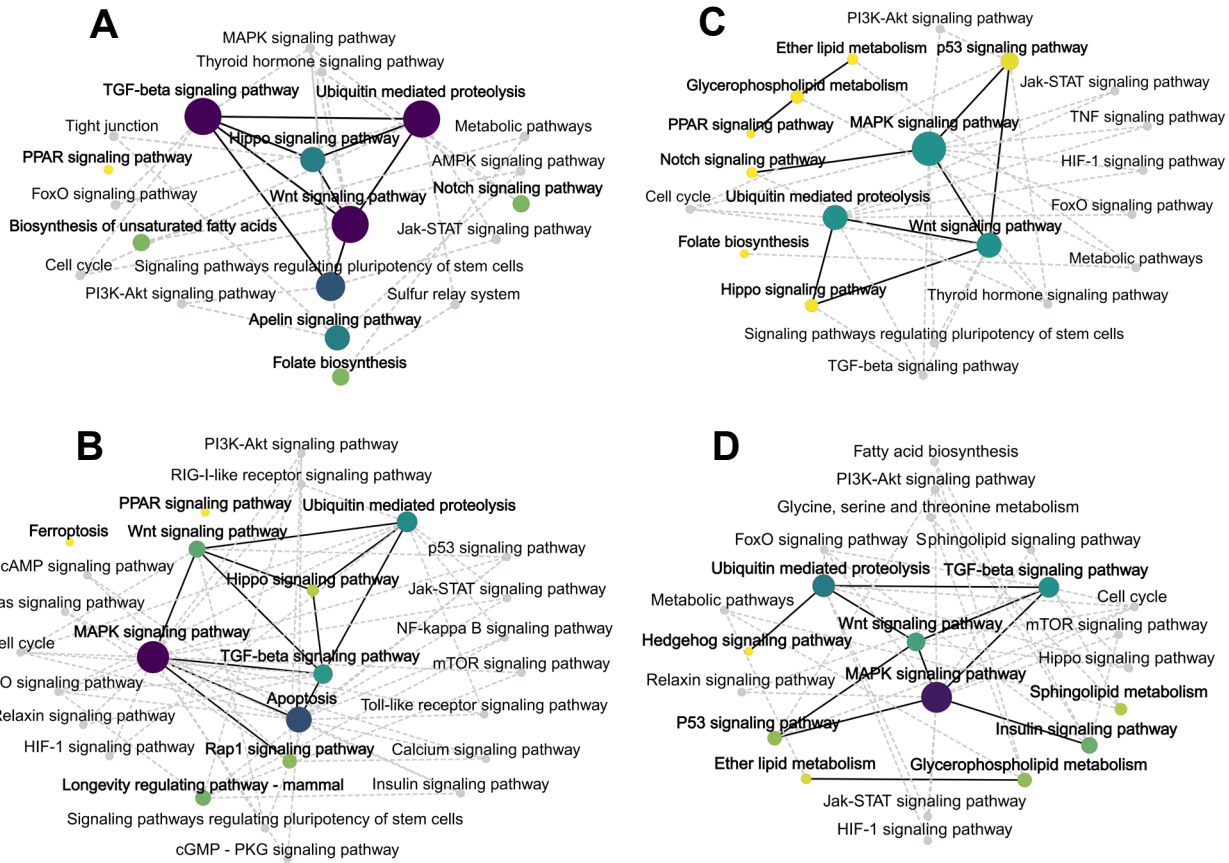
A
MAPK signaling pathway
Thyroid hormone signaling pathway
TGF-beta signaling pathway
Ubiquitin mediated proteolysis
Tight junction
Metabolic pathways
Hippo signaling pathway
PPAR signaling pathway
AMPK signaling pathway
FoxO signaling pathway
Notch signaling pathway
Wnt signaling pathway
Biosynthesis of unsaturated fatty acids
Jak-STAT signaling pathway
Cell cycle
Signaling pathways regulating pluripotency of stem cells
PI3K-Akt signaling pathway
Sulfur relay system
Apelin signaling pathway
Folate biosynthesis
C
PI3K-Akt signaling pathway
Ether lipid metabolism
p53 signaling pathway
Glycerophospholipid metabolism
Jak-STAT signaling pathway
PPAR signaling pathway
MAPK signaling pathway
TNF signaling pathway
Notch signaling pathway
HIF-1 signaling pathway
Cell cycle
Ubiquitin mediated proteolysis
FoxO signaling pathway
Wnt signaling pathway
Folate biosynthesis
Metabolic pathways
Hippo signaling pathway
Thyroid hormone signaling pathway
Signaling pathways regulating pluripotency of stem cells
TGF-beta signaling pathway
B
PI3K-Akt signaling pathway
RIG-I-like receptor signaling pathway
PPAR signaling pathway
Ubiquitin mediated proteolysis
Ferroptosis
Wnt signaling pathway
p53 signaling pathway
cAMP signaling pathway
Hippo signaling pathway
Jak-STAT signaling pathway
Ras signaling pathway
MAPK signaling pathway
NF-kappa B signaling pathway
Cell cycle
TGF-beta signaling pathway
mTOR signaling pathway
FoxO signaling pathway
Apoptosis
Toll-like receptor signaling pathway
Relaxin signaling pathway
HIF-1 signaling pathway
Rap1 signaling pathway
Calcium signaling pathway
Longevity regulating pathway - mammal
Insulin signaling pathway
Signaling pathways regulating pluripotency of stem cells
cGMP - PKG signaling pathway
D
Fatty acid biosynthesis
PI3K-Akt signaling pathway
Glycine, serine and threonine metabolism
FoxO signaling pathway
Sphingolipid signaling pathway
Ubiquitin mediated proteolysis
TGF-beta signaling pathway
Metabolic pathways
Cell cycle
Wnt signaling pathway
mTOR signaling pathway
Hedgehog signaling pathway
Hippo signaling pathway
Relaxin signaling pathway
MAPK signaling pathway
Sphingolipid metabolism
P53 signaling pathway
Insulin signaling pathway
Ether lipid metabolism
Glycerophospholipid metabolism
Jak-STAT signaling pathway
HIF-1 signaling pathway
E
Rap1 signaling pathway
Phospholipase D signaling pathway
AGE-RAGE signaling pathway in diabetic complications
Jak-STAT signaling pathway
Apoptosis
AMPK signaling pathway
Estrogen signaling pathway
TGF-beta signaling pathway
Cell cycle
Notch signaling pathway
cGMP - PKG signaling pathway
FoxO signaling pathway
Relaxin signaling pathway
Wnt signaling pathway
MAPK signaling pathway
Ubiquitin mediated proteolysis
PPAR signaling pathway
Metabolic pathways
Signaling pathways regulating pluripotency of stem cells
Ras signaling pathway
Nicotinate and nicotinamide metabolism
Insulin signaling pathway
HIF-1 signaling pathway
PI3K-Akt signaling pathway
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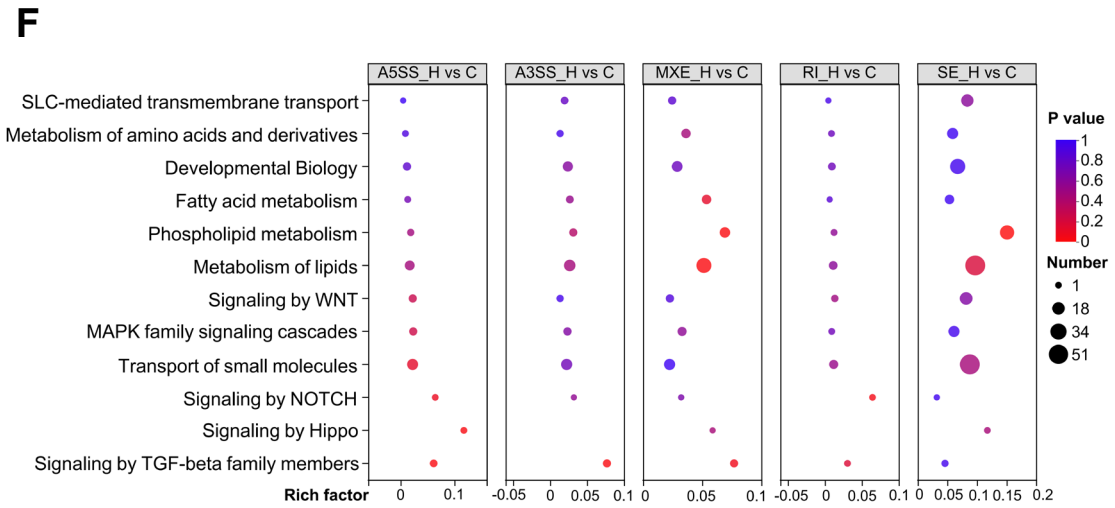
Biosynthesis of unsaturated fatty acids
p53 signaling pathway
Hippo signaling pathway
Sphingolipid signaling pathway



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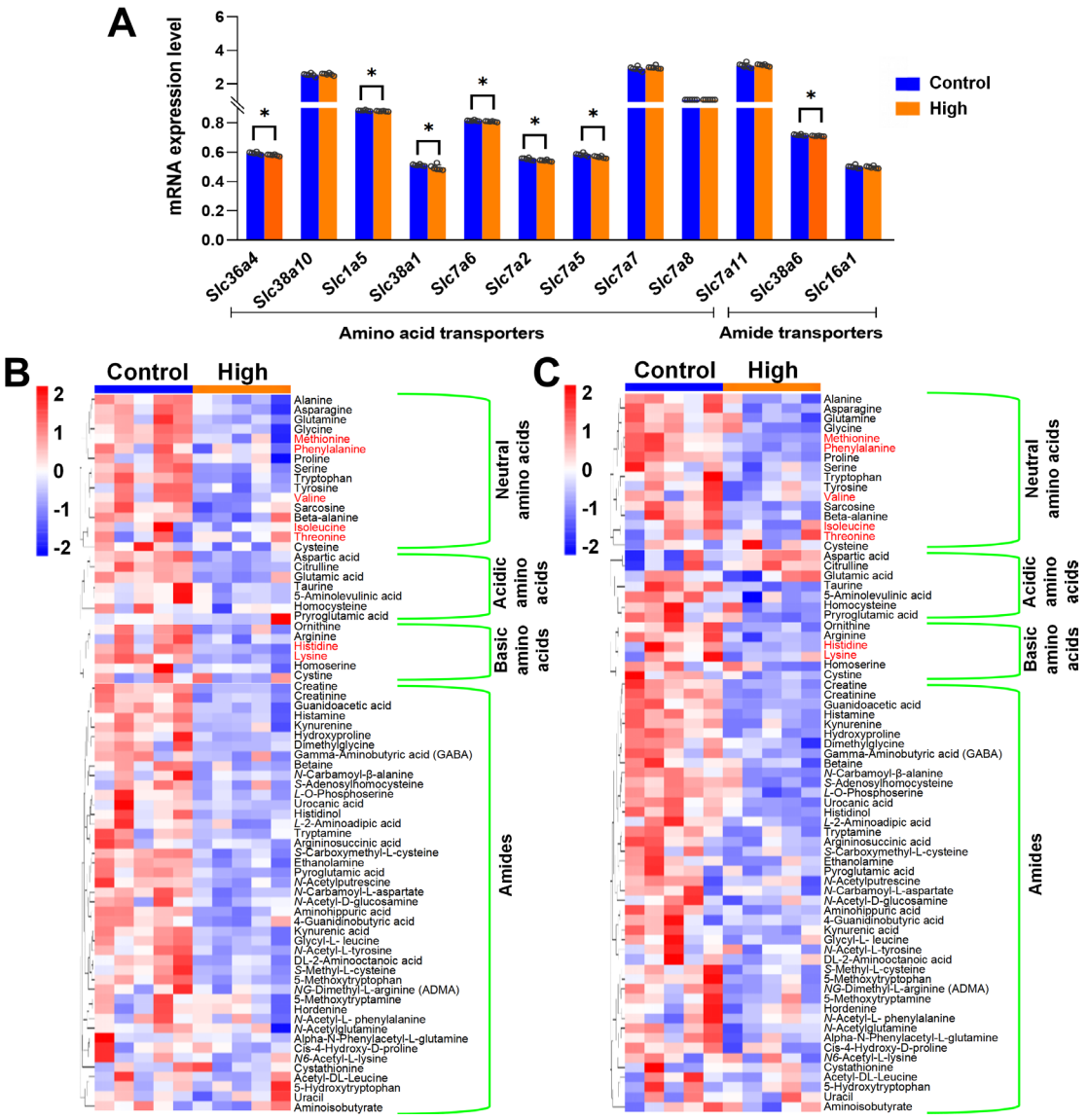

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